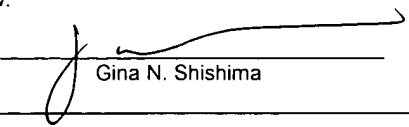




CERTIFICATE OF MAILING
37 C.F.R. §1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Mail Stop AF, Commissioner for Patents, Washington, DC 20231, on the date below:

July 28, 2003
Date


Gina N. Shishima

23
JVI
8/6/03

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

BRIAN F. TACK, PAUL B. MCCRAY,
MICHAEL WELSH, SUE M. TRAVIS AND
ROBERT LEHRER

Serial No.: 09/642,744

Filed: AUGUST 18, 2000

For: ALPHA HELICAL PEPTIDES WITH
BROAD SPECTRUM ANTIMICROBIAL
ACTIVITY THAT ARE INSENSITIVE TO
SALT

Group Art Unit: 1646

Examiner: KHATOL SHAHNAN-SHAH

Atty. Dkt. No.: IOWA:026US/SLH

DECLARATION UNDER 37 C.F.R. §1.132

I, Andrew D. Robertson, do declare that:

1. I currently hold the position of Professor in the Department of Biochemistry at the University of Iowa, Iowa City, IA. My education and training includes an undergraduate degree in Biology from the University of California-San Diego and a Ph.D. in Biochemistry from the University of Wisconsin-Madison. I have authored 40 papers in

the fields of peptides and proteins. Therefore, I consider myself one of ordinary skill in the art of peptide biology.

2. I have reviewed the specification and pending claims for the above-referenced case. In particular, I have focused on the limitation in the pending claims of peptides of 12-37 residues in length. The specification application clearly discloses a family of anti-bacterial peptides which range in size from 12 to 37 residues in length. Thus, it is my opinion that that one of ordinary skill in the art would readily acknowledge that the inventors described in the specification the genus of peptides now being claimed.
3. I hereby declare that all statements made of my own knowledge are true and all statements made on information are believed to be true and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of this application or any patent issued thereon.

July 1, 2003
Date

Andrew D. Robertson
Andrew D. Robertson

CURRICULUM VITAE

ANDREW D. ROBERTSON, Ph.D.
DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF IOWA
IOWA CITY, IA 52242
TEL: 319-335-6515; EMAIL: ANDY-ROBERTSON@UIOWA.EDU

July 27, 2003

I. EDUCATIONAL AND PROFESSIONAL HISTORY

A. List of institutions attended

1981	B.A.	Biochemistry and Cell Biology University of California, San Diego
1988	Ph.D	Biochemistry University of Wisconsin, Madison (Dr. John L. Markley)
1988-1991	Postdoctoral Fellow	Stanford University (Dr. Robert L. Baldwin)

B. Professional and Academic Appointments

1991-1996	Assistant Professor	Department of Biochemistry University of Iowa
1996-2002	Associate Professor	Department of Biochemistry University of Iowa
01/00-03/00	Visiting Assoc. Professor	Division of Chemistry & Chemical Engineering California Institute of Technology
01/01-06/01	Visiting Scientist	Division of Structural Studies MRC Laboratory of Molecular Biology Cambridge, UK
2001-2002	Associate Professor	Division of Medicinal & Natural Products Chemistry University of Iowa
2002-present	Professor	Department of Biochemistry University of Iowa
2002-present	Professor	Division of Medicinal & Natural Products Chemistry

University of Iowa

Other Employment Pertaining to Current Professional Appointments

1991-1994 Director, NMR Facility College of Medicine, University of Iowa

C. Honors, Awards, Recognitions, Outstanding Achievements

1982-1985 NIH Training Grant (predoctoral)
 1988-1990 Postdoctoral Fellow, Damon Runyon-Walter Winchell Cancer Fund
 1993 Lilly Biochemistry Grantee, Eli Lilly and Company

II. TEACHING**A. Teaching Assignments**

<i>Year</i>	<i>Course No.</i>	<i>Title</i>	<i>Length</i>	<i>No. of Students</i>
Spring '92	99:140	Experimental Biochemistry	15 hrs.	20
Fall '92	99:237	Special Topics: NMR in Biochemistry	15 hrs.	11
Spring '93	99:140	Experimental Biochemistry	15 hrs.	14
Fall '93	99:161/162	Biochemistry for Dental and Pharmacy Students	15 hrs.	193
Spring '94	99:140	Experimental Biochemistry	15 hrs.	41
Fall '94	99:120	Biochemistry & Molecular Biology I	15 hrs.	158
Spring '95	99:140	Experimental Biochemistry	15 hrs.	29
Fall '95	99:120	Biochemistry & Molecular Biology I	17 hrs.	142
Fall '95	99:241	Biophysical Chemistry I	15 hrs.	17
Fall '96	99:120	Biochemistry & Molecular Biology I	15 hrs.	118
Fall '96	99:241	Biophysical Chemistry I	15 hrs.	17
Fall '97	99:120	Biochemistry & Molecular Biology I	15 hrs.	115
Fall '97	99:241	Biophysical Chemistry I	15 hrs.	8
Fall '98	99:241	Biophysical Chemistry I	15 hrs.	28
Fall '98	50:162	Foundations of Clinical Practice, CBL	10 hrs.	7
Fall '99	99:241	Biophysical Chemistry I	15 hrs.	12
Fall '99	50:162	Foundations of Clinical Practice, CBL	10 hrs.	7
Winter '00	Ch 24a	Intro. to Biophys. Chem. (Calif Inst. Tech.)	30 hrs.	34
Fall '00	99:241	Biophysical Chemistry I	15 hrs.	24
Fall '00	50:162	Foundations of Clinical Practice, CBL	10 hrs.	7
Fall '01	99:241	Biophysical Chemistry I	15 hrs.	25
Fall '01	50:162	Foundations of Clinical Practice, CBL	10 hrs.	7
Fall '02	99:241	Biophysical Chemistry I	15 hrs.	41
Fall '02	50:162	Foundations of Clinical Practice, CBL	10 hrs.	6
Fall '02	02:170	Intro. To Bioinformatics	4 hrs.	35
Fall '03	99:241	Biophysical Chemistry I	15 hrs.	
Fall '03	02:170	Intro. To Bioinformatics	4 hrs.	
Spring '04	99:237	NMR of Biomacromolecules	15 hrs.	

Teaching Activities other than classroom or clinical, including teaching of undergraduate (pre-baccalaureate), graduate, and post-doctoral students and continuing education.

Two undergraduates, two graduate students, and one postdoctoral trainee are training in my laboratory.

Spring '98 - Participated in a four-day workshop, Technology in the Learning Environment, offered by U. of Iowa Center for Teaching, Information Technology Services, and the University Libraries

04/26/99 - Organized and conducted Workshop on Desktop Molecular Modeling
College of Medicine Research Week

B. Students and Staff supervised

Currently supervised

Michael Chimenti (2002-present)	Undergraduate Research
Debra Ferraro (2001-present)	Graduate Student
Gary Heil (2002-present)	Postdoctoral Trainee
Andrew Houk (2002-present)	Laboratory Assistant
Nicole Iverson (2002-present)	Research Assistant I
Andrea Schoenfish (2001-present)	Laboratory Assistant
Navdeep Sidhu (2001-present)	Graduate Student

Previously supervised

Cammon Arrington (1996-2000)	Graduate Student (MSTP)
Sarah Aeilts (1996-1997)	Laboratory Assistant
Jon Barry (1995)	Undergraduate (Carlton College)
Peter Bowers (1991-1992)	Undergraduate (Biochemistry, Honors)
Ben Buscher (1994-1995)	Laboratory Assistant
Gregory DeKoster (1991-1997)	Graduate Student
Jennifer Elwood (1999-2001)	Research Assistant I
Thomas Fabricius (1995)	Medical Student/Student Research Fellow
Christopher Fore (1993-1994)	Undergraduate (Biochemistry, Honors)
William Forsyth (1994-1999)	Graduate Student
Jay Hesselberth (1996-1997)	Undergraduate Research
Trina Hudson (1997-1998)	Undergraduate Research
Rainbo Hultman (1999-1999)	Laboratory Assistant
Nicole Iverson (1999-2002)	Research Assistant I
William Kearney (1992-1994)	Assistant Research Scientist
Mark Klein (1996)	Medical Student/Student Research Fellow
Jana Klingbeil (1992-1994)	Laboratory Assistant
Noel Lazo (2002)	Assistant Research Scientist
Juanita Limas (1991-1993)	Laboratory Assistant
Ting Liu (1998-2000)	Graduate Student
Jennifer McCoy (1995-1996)	Laboratory Assistant
Scott Penisten (1992)	Undergraduate (Biochemistry)
Nadia Sabbagh (1998)	Laboratory Assistant
Wolfgang Schaller (1992-1993)	Graduate Student (Biochemistry)

Stephanie Schmid (1997-1998)	Undergraduate Research
T. Sivaraman (1999-2001)	Postdoctoral Trainee
Johnette Snyder (1999-2001)	Laboratory Assistant
Monica Sundd (2000-2002)	Postdoctoral Trainee
Kyle Ver Steeg (1995)	Undergraduate (Biochemistry)
Liskin Swint-Kruse (1991-1995)	Graduate Student (Biochemistry)
Timothy Volm (1998)	Postdoctoral trainee
Jeremy Weis (1998-1999)	Undergraduate Research

Graduate Student Rotations

Andrew Thomas	2003 (Biosciences)
Brian Gilmore	2002
Navdeep Sidhu	2001
Debra Ferraro	2000
Jared Helm	2000
Rhonda Thomas	2000
Douglas Summerfield	2000
Iwona Wyka	1999
Benjamin Darbro	1999 (MSTP)
Wendy VanScyoc	1999
Sarah Shore	1999
Elena Kovaleva	1998
Jason-Thomas Eppel	1998
Amy Siegling	1998
Ting Liu	1998
James Horn	1997
Jon Rubach	1996
Dong-Mei Cheng	1996
Robert Walters	1996 (MSTP)
Olav Jaren	1996 (MSTP)
Carrie Barnes	1996
Stephen Edgcomb	1996
Addison Ault	1995
Cam Arrington	1995 (MSTP)
Andre Walther	1995
Junmin Peng	1995
Douglas Bartels	1995
Kuo-Kuang Wen	1994
Shawna Biddle	1994 (MSTP)
William Forsyth	1994
Brian Baker	1994
Debbie Thurmond	1993
Victoria Robinson	1993
Anthony Lackey	1992
Gregory DeKoster	1991
Liskin Swint	1991

Masters and Ph.D. Theses Directed and Postdoctoral Fellows Supervised

Cammon B. Arrington	Ph.D. (2001)
Gregory T. DeKoster	Ph.D. (1997)
William R. Forsyth	M.S. (1996), Ph.D. (1999)
Monica Sundd	Postdoc. Trainee (2000-2002)
T. Sivaraman	Postdoc. Trainee (1999-2001)
Liskin Swint-Kruse	Ph.D. (1995)
Wolfgang Schaller	M.S. (1993)
Timothy Volm	Postdoc. Trainee (1998)

Thesis Committees

Youngbae Kim	2003-present (Chemistry)
Ling Song	2002-present
Elena Kovaleva	2000-present
Sarah Shore	2000-present
Iwona Wyka	2002-2003 (M.S.)
Wendy van Scyoc	2001-2003
James Horn	1998-2002
Matthew Emig	1996-2001 (Microbiology)
Olav Jaren	1998-2001
Stephen Edgcomb	1996-2001
Qin Zou	1997-2000
Andre Walther	1996-2000
Doug Bartels	1996-1999
Samuel Dagorne	1998-1999 (Chemistry)
Wei Xu	1999
Rohit Medheker	1998-1999 (Chemistry)
Mehrdad Pedram	1996-1999
Laurie LeBrun	1994-1999
James Dean	1994-1999
Katherine Braun	1996-1998
Barbara Tsuie	1997-1998 (Chemistry)
Heeyeong Cho	1996-1997
Kevin Latinis	1995-1997 (Immunology Program)
Brian Baker	1995-1997
Victoria Robinson	1994-1997
Brenda Sorensen	1994-1997
Joseph Christopher	1996-1997 (Chemistry)
Li Feng	1995-1996
David Black	1995-1996 (Chemistry)
Susan Habermann	1996
Xavier Gomes	1993-1996
Gary Quinby	1992-1995
David Chafin	1991-1995
Pramod Wangikar	1993-1995 (Chem. & Biochem. Eng.)
Susan Pedigo	1992-1995

David Mitchell	1991-1995
Sangkee Rhee	1991-1994
Stephan Rodewald	1993-1994 (Chemistry)
Daniel Kephart	1991-1994
Samuel Borkowsky	1991-1992 (Chemistry)

III. SCHOLARSHIP

A. *Peer-Reviewed Publications*

1. Warner, T.G., Robertson, A.D. and O'Brien, J.S. (1983) Diagnosis of GM₁ gangliosidosis based on detection of urinary oligosaccharides with high performance liquid chromatography. *Clinica Chimica Acta* **127**:313-326.
2. Warner, T.G., Robertson, A.D., Mock, A.K., Johnson, W.G. and O'Brien, J.S. (1983) Prenatal diagnosis of GM₁ gangliosidosis by detection of galactosyl-oligosaccharides in amniotic fluid with high-performance liquid chromatography. *American J. of Human Genetics* **35**:1034-1041.
3. Hoover, T.R., Robertson, A.D., Cerny, R.L., Hayes, R.N., Imperial, J., Shah, V.K. and Ludden, P.W. (1987) Identification of the V factor required for synthesis of the iron-molybdenum cofactor of nitrogenase as homocitrate. *Nature* **329**:855-857.
4. Anderson, M.S., Robertson, A.D., Macher, I. and Raetz, C.R.H. (1988) Biosynthesis of lipid A precursors: *in vitro* formation of UDP-2,3-diacyl-GlcN from UDP-3-O-acyl-GlcNAc proceeds by way of UDP-3-O-acyl-glucosamine. *Biochemistry* **27**:1908-1917.
5. Robertson, A.D., Westler, W.M. and Markley, J.L. (1988) Two-dimensional NMR studies of Kazal proteinase inhibitors. 1. Sequence-specific assignments and secondary structure of turkey ovomucoid third domain. *Biochemistry* **27**:2519-2529.
6. Brasaemle, D.B., Robertson, A.D. and Attie, A.D. (1988) Transbilayer movement and distribution of cholesterol in human erythrocytes. *J. of Lipid Research* **29**:481-489.
7. Brozek, K.A., Hosaka, K., Robertson, A.D. and Raetz, C.R.H. (1989) Biosynthesis of lipopolysaccharide in *Escherichia coli*: Cytoplasmic enzymes that attach 3-deoxy-D-manno-octulosonic acid to lipid A. *J. of Biological Chemistry* **264**:6956-6966.
8. Robertson, A.D., Purisima, E.O., Eastman, M.A. and Scheraga, H.A. (1989) Proton NMR assignments and regular backbone structure of bovine pancreatic ribonuclease A in solution. *Biochemistry* **28**:5930-5938.
9. Robertson, A.D., Rhyu, G.K., Westler, W.M. and Markley, J.L. (1990) Assignment of the carbon-13 NMR spectra of virgin and reactive-site modified turkey ovomucoid third domain. *Biopolymers* **29**:461-467.
10. Shoemaker, K.R., Fairman, R., Schultz, D.A., Robertson, A.D., York E.J., Stewart, J.M. and Baldwin, R.L. (1990) Sidechain interactions in the C-peptide helix: Phe8...His 12. *Biopolymers* **29**:1-11.
11. Strehlow, K.G., Robertson, A.D. and Baldwin, R.L. (1991) Proline for alanine substitutions in the C-peptide helix. *Biochemistry* **30**:5810-5814.
12. Robertson, A.D. and Baldwin, R.L. (1991) Hydrogen exchange in thermally denatured ribonuclease A. *Biochemistry* **30**:9907-9914.

13. Swint, L. and Robertson, A.D. (1993) Thermodynamics of unfolding for turkey ovomucoid third domain: Thermal and chemical denaturation. *Protein Science* **2**:2037-2049.
14. Krezel, A.M., Darba, P., Robertson, A.D., Fejzo, J., Macura, S., and Markley, J.L. (1994) Solution structure of turkey ovomucoid third domain as determined from nuclear magnetic resonance data. *Journal of Molecular Biology* **242**:203-214.
15. Schaller, W. and Robertson, A.D. (1995) pH, ionic strength and temperature dependences of ionization equilibria for the carboxyl groups in turkey ovomucoid third domain. *Biochemistry* **34**:4714-4723.
16. Swint-Kruse, L. and Robertson, A.D. (1995) Hydrogen bonds and the pH dependence of ovomucoid third domain stability. *Biochemistry* **34**:4724-4732.
17. DeKoster, G.T. and Robertson, A.D. (1995) Cold denaturation of CheY. *Journal of Molecular Biology* **249**:529-534.
18. Wang, A., Robertson, A.D., and Bolen, D.W. (1995) Effects of a naturally occurring compatible osmolyte on the internal dynamics of ribonuclease A. *Biochemistry* **34**:15096-15104.
19. Swint-Kruse, L. and Robertson, A.D. (1996) Temperature and pH dependences of hydrogen exchange and global stability for ovomucoid third domain. *Biochemistry* **35**:171-180.
20. Forsyth, W.R. and Robertson, A.D. (1996) Intramolecular electrostatic interactions accelerate hydrogen exchange in diketopiperazine relative to 2-piperidone. *J. American Chemical Society* **118**:2694-2698.
21. DeKoster, G.T. and Robertson, A.D. (1997) Thermodynamics of unfolding for Kazal-type serine protease inhibitors: Entropic stabilization of ovomucoid first domain by glycosylation. *Biochemistry* **36**:2323-2331.
22. DeKoster, G.T. and Robertson, A.D. (1997) Calorimetrically-derived parameters for protein interactions with urea and guanidine-HCl are not consistent with denaturant m values. *Biophys. Chem.* **64**:59-68.
23. Arrington, C.B. and Robertson, A.D. (1997) Microsecond protein folding kinetics from native state hydrogen exchange. *Biochemistry* **36**:8686-8691.
24. Robertson, A.D. and Murphy, K.P. (1997) Protein structure and the energetics of protein stability. *Chemical Reviews* **97**:1251-1268 (Invited submission, subjected to peer-review).
25. Forsyth, W.R., Gilson, M.K., Antosiewicz, J., Jaren, O.R., and Robertson, A.D. (1998) Theoretical and experimental analysis of ionization equilibria in ovomucoid third domain. *Biochemistry* **37**:8643-8652.
26. Arrington, C.B., Teesch, L.M. and Robertson, A.D. (1999) Defining protein ensembles with native-state NH exchange: Kinetics of interconversion and cooperative units from combined NMR and MS analysis. *Journal of Molecular Biology* **285**:1265-1275.
27. Liu, T., Pemberton, P.A., and Robertson, A.D. (1999) Three-state unfolding and self-association of maspin, a tumor-suppressing serpin. *Journal of Biological Chemistry* **274**:29628-29632.
28. Arrington, C.B. and Robertson, A.D. (2000) Microsecond to minute dynamics revealed by EX1-type hydrogen exchange at nearly every backbone hydrogen bond in a native protein. *Journal of Molecular Biology* **296**:1307-1317.

29. Ostedgaard, L.S., Baldursson, O., Vermeer, D.W., Welsh, M.J., and Robertson, A.D. (2000) A functional R domain from CFTR is predominantly unstructured in solution. *Proceedings of the National Academy of Sciences U.S.A.* **97**:5657-5662.
30. Forsyth, W.R. and Robertson, A.D. (2000) Insensitivity of perturbed carboxyl pK values in ovomucoid third domain to charge replacement at a neighboring residue. *Biochemistry* **39**: 8067-8072.
31. Arrington, C.B. and Robertson, A.D. (2000) Correlated motions in native proteins from MS analysis of NH exchange: Evidence for a manifold of unfolding reactions in ovomucoid third domain. *Journal of Molecular Biology* **300**: 221-232.
32. Sivaraman, T., Arrington, C.B., and Robertson, A.D. (2001) Kinetics of unfolding and folding from amide hydrogen exchange in native ubiquitin. *Nature Struct. Biol.* **8**: 331-333.
33. Rees, D.C. and Robertson, A.D. (2001) Some thermodynamic implications for the thermal stability of proteins. *Prot. Sci.* **10**: 1187-1194.
34. Rodriguez, H.M., Robertson, A.D. and Gregoret, L.M. (2002) Hairpin-directed folding of *E. coli* CspA, a small β -sheet protein. *Biochemistry* **41**: 2140-2148.
35. Tack, B.F., Sawai, M.V., Kearney, W.R., Robertson, A.D., Sherman, M.A., Wang, W., Hong, T., Boo, L.M., Wu, H., Waring, A.J., and Lehrer, R.I. (2002) SMAP-29 has two LPS-binding sites and a central hinge. *European Journal of Biochemistry* **269**: 1-9.
36. Li, H., Hains, A.W., Everts, J.E., Robertson, A.D., and Jensen, J.H. (2002) The prediction of protein pK_a's using QM/MM: The pK_a of lysine 55 in turkey ovomucoid third domain. *Journal of Physical Chemistry B* **106**: 3486-3494.
37. Forsyth, W.R., Antosiewicz, J., and Robertson, A.D. (2002) Empirical relationships between protein structure and carboxyl pK_a values in proteins. *Proteins* **48**: 388-403.
38. Sundd, M., Iverson, N., Ibarra-Molero, B., Sanchez-Ruiz, J.M., and Robertson, A.D. (2002) Electrostatic interactions in ubiquitin: Stabilization of carboxylates by lysine amino groups. *Biochemistry* **41**: 7586-7596.
39. Sundd, M. and Robertson, A.D. (2003) Rearrangement of charge-charge interactions in variant ubiquitins as detected by Double-Mutant Cycles and NMR. *Journal of Molecular Biology*, in press.

Non-Peer-Reviewed Publications

1. Robertson, A.D. and Markley, J.L. (1990) ¹H NMR Methods for Protein Spectral Assignments in *Biological Magnetic Resonance* **9**:155-176. L.J. Berliner and J. Reuben, eds., Plenum Press, New York.
2. DeKoster, G.T., Robertson, A.D., Stock, A.M. and Stock, J.B. (1993) Urea and guanidine-HCl yield different unfolding free energies for CheY: Which denaturant provides the most reliable free energy values? *Techniques in Protein Chemistry IV*. R.H. Angeletti, ed., Academic Press, New York, pp. 533-540.
3. Scholtz, J.M. and Robertson, A.D. (1995) Hydrogen exchange techniques in *Meth. Molec. Biol.* **40**: 291-311.

4. Welsh, M.J., Robertson, A.D., and Ostedgaard, L.S. (1998) The ABC of a versatile engine. *Nature* **396**:623-624.
5. Arrington, C.B. and Robertson, A.D. (2000) Kinetics and thermodynamics of conformational equilibria in native proteins by hydrogen exchange. *Meth. Enzymology* **323**: 104-124.
6. Sivaraman, T. and Robertson, A.D. (2001) Kinetics of conformational fluctuations by EX1 hydrogen exchange in native proteins in *Meth. Molec. Biol.* **168**: 193-214.
7. Sundd, M. and Robertson, A.D. (2002) Illuminating proteins with Aladan's Lamp. *Nature Struct. Biol.* **9**: 500-501. (News and Views).
8. Robertson, A.D. (2002) Intramolecular interactions at protein surfaces and their impact on protein function. *Trends in Biochemical Sciences* **27**: 521-526.

Submitted

1. Li, H., Robertson, A.D. and Jensen, J.H. (2003) The determinants of carboxyl pK_a values in turkey ovomucoid third domain. Submitted to *Proteins*.
2. Bilodeau, P.S., Winistorfer, S.C., Kearney, W.R., Robertson, A.D., and Piper, R.C. (2003) Cooperation of the Vps27-Hse1 and ESCRT-I complexes for sorting ubiquitinated proteins at the endosome. Submitted to *Journal of Cell Biology*.

In Preparation

1. Lazo, N., Ferraro, D.M. and Robertson, A.D. (2003) Hydrogen exchange and protein folding. To be submitted to *Biochemistry* (Review).
2. Sivaraman, T., Ferraro, D.M. and Robertson, A.D. (2003) The relationship between folding and slow hydrogen exchange in ubiquitin. To be submitted to *Biochemistry*.
3. Robertson, A.D. and Chothia, C. (2003) Sequence determinants of the ubiquitin fold. To be submitted to *Proceedings of the National Academy of Sciences*.
4. Iverson, N., Ramaswamy, S. and Robertson, A.D. (2003) The 1 Å crystal structure of a single-site variant of mammalian ubiquitin. To be submitted to *Acta Crystallography D*.

B. Areas of Research Interest

Molecular Basis for Slow Amide Hydrogen Exchange in Proteins. Amide hydrogen exchange is a popular tool for the study of protein structure, dynamics and function. The advent of mass spectrometry (MS) measurements of hydrogen-deuterium exchange has expanded the applications of exchange to a wide variety of questions in protein structure and function. In spite of its widespread use, significant questions remain regarding the molecular interpretation of exchange data. Our laboratory has focused much of its attention on the molecular mechanisms governing slow exchange of amide hydrogens from proteins. We are using multidimensional NMR, MS, computation and mutagenesis to identify the types of motions leading to exchange as well as other factors, such as steric clash, that can impede exchange at otherwise solvent-exposed amide groups. We have also begun using exchange as measured by MS to investigate the structure and function of large proteins and macromolecular complexes

such as molecular motors. Our long-term goal is to identify the correlated or concerted motions that are key to the biological function of these molecular machines.

Physics and Chemistry at Protein Surfaces. Most of protein function, from catalysis to assembly of macromolecular complexes, involves the solvent-exposed surfaces of proteins. Despite the biological significance of protein surfaces and rapidly expanding knowledge of protein structure, protein surfaces are a mystery with respect to intramolecular interactions among side chains and the conformations of these side chains. To what extent do residues at protein surfaces interact with one another? Do solvent-exposed side chains adopt a single conformation, a set of conformations or are they rapidly sampling a wide variety of conformations? Answers to these questions are needed for a more complete understanding of structure-function relationships in proteins. Our research addresses these questions in ubiquitin and ubiquitin-like proteins by combining pK determinations at nearly all ionizable groups with mutagenesis, computation and structure determination by both x-ray and NMR. Ionizable residues make up as much as 40% of all surface residues in globular proteins and their pKs are thus one of the few experimental reporters on structure and energetics at multiple surface residues. Moreover, and contrary to what many might think, pKs for surface residues are often not equal to model compound values. Mutational studies reveal significant interactions among solvent-exposed side chains. Moreover, for specific pairwise interactions we are beginning to identify the role played by other residues in modulating these interactions.

C. Grants received

Previous:

University of Iowa Cancer Center
\$ 15,000
10/01/91 -09/30/92
A.D. Robertson, P.I.

“Determination of Protein Structure by Nuclear Magnetic Resonance Spectroscopy”
Central Investment Fund for Research Enhancement
University of Iowa
\$ 6,356
01/01/95 - 06/30/95
A.D. Robertson, P.I.

1993 Lilly Biochemistry Grantee
Eli Lilly and Company
\$ 20,000
08/01/93 - 07/31/95
A.D. Robertson, P.I.

“Purchase of an Analytical Ultracentrifuge”
National Institutes of Health, S10 RR10409-01A1
\$233,644
04/01/96 - 03/31/97

R.E. Cohen, P.I.
Co-P.I. with 9 other Co-P.I.'s

"Conformational Dynamics and Thermal Stability of Proteins"
National Institutes of Health, R01 GM46869-01 to -05
\$422,945
02/01/92 - 07/31/97
A.D. Robertson, P.I.
45% effort, 20% salary support

"Conformational Dynamics and Thermal Stability of Proteins"
National Institutes of Health, R01 GM46869-06 to -09
\$432,000
08/01/97- 07/31/2001
A.D. Robertson, P.I.
30% effort, 25% salary support

"Molecular Architecture of SLP-76, the Adapter Protein Essential for T-Cell Development and Receptor Signaling"
University of Iowa Biosciences Initiative
\$50,000
01/01/99 - 06/30/99
G.A. Koretzsky, A.D. Robertson, M.A. Shea, Co-P.I.'s
This is a pilot grant to initiate a collaborative study of SLP-76.

Purchase of an LC-MS-MS Instrument
National Institutes of Health, S10 RR13799-01
\$221,400
04/01/99 - 03/31/00
J.B. Gloer, P.I.
Co-P.I. with 7 other Co-P.I.'s

SCOR in Airway Biology and Pathogenesis of Cystic Fibrosis
National Institutes of Health
\$923,765 (\$5,723,394 total direct for SCOR)
09/30/98 - 09/29/02
M.J. Welsh, Director
10% effort, 10% salary; A.D. Robertson is a co-investigator on one of the 5 projects
A.D. Robertson would work with a postdoctoral trainee to determine the solution structure of a domain in the protein CFTR.

Active:

"Conformational Dynamics and Thermal Stability of Proteins"
National Institutes of Health, RO1 GM46869-10 to -13
\$747,904
08/01/01- 07/31/2005

A.D. Robertson, P.I.
30% effort, 30% salary support

Pending:

"Chemistry and Physics at Protein Surfaces"
National Institutes of Health, R01 GM66846-01 to -05
\$1,125,000
A.D. Robertson, P.I.

E. Invited Lectures and Conference Presentations

09/30/91	Luther College, Department of Chemistry
11/18/91	University of Missouri-Columbia, Department of Biochemistry
05/07/92	Iowa State University, Department of Biochemistry and Biophysics
06/04/93	Midwest Biotechnology Symposium, Minneapolis, MN
11/11/93	28 th American Chemical Society Midwest Regional Meeting, Columbia, MO
04/26/94	University of Utah, Department of Chemistry
06/29/94	Biopolymers Gordon Conference
09/06/94	University of Texas Health Science Center at San Antonio, Department of Biochemistry
09/08/94	University of Texas Medical Branch at Galveston, Department of Human Biological Chemistry & Genetics
10/28/94	Princeton University, Department of Chemistry
11/10/94	Eli Lilly and Co., Indianapolis, IN
05/17/95	Washington University School of Medicine, Department of Biochemistry and Molecular Biophysics
10/25/95	Texas A & M University, Department of Biochemistry and Biophysics
02/19/96	University of Wisconsin-Madison, Department of Biochemistry
04/19/96	Southern Illinois University, Department of Medical Biochemistry
03/18/97	The Second Johns Hopkins Protein Folding Meeting (Discussion Leader)
03/20/97	Johns Hopkins University, Department of Biology
03/21/97	Center for Advanced Research in Biotechnology, Rockville, MD
08/04/97	52 nd Annual Calorimetry Conference, Asilomar, CA
10/06/97	11 th Annual Gibbs Conference on Biothermodynamics, Carbondale, IL
10/20/97	Northern Illinois University, Department of Chemistry
10/30/97	California Institute of Technology, Department of Biology
02/04/98	Grinnell College, Department of Chemistry
02/09/98	Purdue University, Program in Biochemistry and Molecular Biology
03/16/98	The Third Johns Hopkins Protein Folding Meeting
03/25/99	Iowa State University, Department of Biochemistry and Biophysics
07/01/99	Cambridge University, Department of Chemistry
07/02/99	Oxford University, Centre for Molecular Sciences
10/20/99	Loras College, Department of Chemistry and Biology
12/02/99	North Carolina State University, Department of Biochemistry
02/08/00	University of California-San Diego, Dept. of Chemistry and Biochemistry
02/22/00	University of California-Santa Cruz, Dept. of Chemistry and Biochemistry
03/09/00	California Institute of Technology, Biochemistry Program

05/03/00 Augsburg College, Department of Chemistry
 08/03/00 Medical University of South Carolina, Department of Cell and
 Molecular Pharmacology
 09/15/00 International EEC Biotechnology Meeting on "Understanding
 Protein Electrostatics", Stockholm, Sweden
 10/24/00 16th Asilomar Conference on Mass Spectrometry, Pacific Grove, CA
 03/01/01 Division of Structural Studies, MRC Laboratory of Molecular Biology,
 Cambridge UK
 11/27/01 University of Vermont College of Medicine, Department of Biochemistry
 01/25/02 Discussion Leader, Gordon Research Conference on Protein Folding and
 Dynamics, Ventura CA
 02/28/02 Laboratory of Persistent Viral Diseases, Rocky Mountain Laboratories, NIAID,
 NIH, Hamilton MT
 03/11/02 University of Massachusetts Medical School, Dept. of Biochemistry &
 Molecular Pharmacology
 04/09/02 223rd ACS National Meeting, "Modern Aspects of Structure Function
 Correlations of Biomolecules: Electrostatic Aspects", Orlando FL
 04/11/02 223rd ACS National Meeting, "Modern Aspects of Structure Function
 Correlations of Biomolecules: Enzyme Action", Orlando FL
 10/14/02 University of Virginia, Biophysics Program, Charlottesville VA
 11/13/02 Butler University, Dept. of Chemistry, Indianapolis IN
 02/24/03 University of British Columbia, Department of Biochemistry, Vancouver,
 Canada
 02/25/03 Simon Fraser University, Dept. of Molecular Biology & Biochemistry,
 Burnaby, Canada
 03/11/03 Mayo Clinic, Department of Biochemistry and Molecular Biology,
 Rochester MN
 03/24/03 ExSAR Corporation, Monmouth Junction NJ
 05/16/03 Pacific Northwest National Laboratory, Biomolecular Systems Initiative,
 Richland WA
 10/08/03 University of Colorado at Boulder, Dept. of Chemistry & Biochemistry

F. Consulting

2002-present NMR Facility at Jackson State University, Jackson MS

IV. SERVICE

A. Offices held in professional organizations

Professional Activities (Boards, Editorships, Study Sections, etc.)

Study Sections

NIH Molecular and Cellular Biophysics Study Section (BBCA)

Ad hoc, 10/99

Special Emphasis Panels

NIH Biophysical Chemistry Study Section, 12/98
 NIH Program Project Proposals, 12/01, 02/02
 Shared Instrument Proposals, 06/02

Meeting Organization

12th Annual Gibbs Conference on Biothermodynamics (1998)

Editorial Advisory Board

Protein Science (1998-2004)

Reviewer: Journals

Biochemistry
 Biophysical Chemistry
 Biophysical Journal
 European Journal of Biochemistry
 FEBS Letters
 Journal of the American Chemical Society
 Journal of the American Society for Mass Spectrometry
 Journal of Biological Chemistry
 Journal of Organic Chemistry
 Journal of Molecular Biology
 Nature Structural Biology
 Protein Science
 Proteins: Structure, Function, and Genetics
 Science

Grant Proposals

American Chemical Society (Ad hoc)
 Central Investment Fund for Research Enhancement, U. of Iowa
 John Sealy Memorial Endowment Fund for Biomedical Research
 at University of Texas Medical Branch at Galveston (1997-present)
 VP for Research (Ad hoc)
 National Science Foundation (Ad hoc)
 Research Corp., Cottrell College Science Awards (Ad hoc)

Textbook

Biochemistry (2nd Ed.) by Mathews and Van Holde (1997)

Other

Review of NMR Resources, U. of Missouri - Columbia (11/99)

Collegiate, University and National Committees

Departmental

Departmental Reading Room Committee (Chair 1991-1992; Member 1997-1998)
 Departmental Seminar Committee (Fall, 1992)
 Departmental Space Committee (1992-1993)
 Graduate Student Admissions and Recruitment (1993-1995; 1997-2000), Chair (1995)

Ph.D. Comprehensive Examination Committee (1993-1995; 2000-2002), Coordinator (1995)
 Faculty Recruiting Committee (1995-1996, 1998-1999, 2002-2003)
 Departmental Equipment Committee (1995-1998)
 Departmental Graduate Studies Committee (1996-1997)
 Teaching & Curriculum Committee (1998-2001; Chair, 2001)
 Undergraduate Advisor (2000-present)
 Faculty Recruiting Committee, Div. of Medicinal & Natural Products Chem., College
 of Pharmacy (2001-2002)

Collegiate

Advisory Committee Chair, College of Medicine NMR Facility (1992-present)
 Advisory Committee for New Teaching Laboratories in the Medical Education
 Building (1992-1993)
 Cancer Center Research Review Committee, Ad hoc (1994)
 MSTP Admissions and Recruiting, Ad hoc (1996-present)
 Interviewer, Medical Student Admissions (1996-present)
 Selection Committee, J.P. Long Basic Science Teaching Award (1997-2000)
 College of Medicine Working Group on Research Facilities (1998)
 Planning Committee for Proposal to Howard Hughes Medical Institute Research
 Resources Program Award (1998)
 Working Group on Synchrotron X-ray Source for Structural Biology (1998-present)
 Review Committee, Dept. of Obstetrics and Gynecology (1999-2000)
 Planning Committee for Medical Education and Biomedical Research Facility-B (2000-present)
 Panel Discussant, New Faculty Orientation, 8/1/02
 Internal Advisory Committee, University of Iowa Center for Immune Mediated Inflammatory
 Disorders (2003-present)

University

Planning Committee for the 10th Biocatalysis and Bioprocessing Conference (2000-2001)
 University of Iowa Biosciences Advisory Panel (2003-2006)

Other Professional Affiliations

American Chemical Society, Younger Chemists Committee (1988-1991)
 American Association for the Advancement of Science
 American Society of Biochemistry and Molecular Biology
 Biophysical Society, Education Committee (1997-2000)
 Protein Society